

REMARKS/ARGUMENTS

Upon entry of this amendment, Claims 25, 30-36, 39-46, and 50-52 are pending. Claims 1-24, 26-29, 37-38, 47-49 and 53-54 are canceled. Claims 1, 8-19, 47-49 and 54 remain canceled without prejudice, as being drawn to non-elected subject matter.

Claims 25, 30, 33, 34 and 44 are amended to correct their dependencies and/or to correct grammatical or typographical errors. Claim 50 is amended to more specifically state that the induced antibodies interfere with the ability of *Neisseria gonorrhoeae* bacteria to adhere to mammalian epithelial cells in a gonococcal cell adherence assay.

The amendments to claim 50 are supported in the present specification, which is the identical disclosure in the priority documents, at pg. 20, lines 26-29; pg. 25, lines 25-30; pg. 26, line 14 through pg. 27, line 2; pg. 35, lines 7-10; and in Example 8 at pg. 53. Note that the antiserum used in Example 8 was developed to the first 178 amino acids of SEQ ID NO: 2. The first 178 amino acids of SEQ ID NO: 2 differ from the first 178 amino acids of SEQ ID NO: 4 by only 3 amino acids. Thus the polypeptide used to immunize the mammalian subjects of the preceding examples falls within the claim language “an isolated polypeptide having an amino acid sequence having 95% or greater sequence identity with the amino acid sequence of SEQ ID NO: 4”.

Claims 34 and 44 are also amended by clarifying that the proteins of the other *Neisseria* bacteria appear as reactive bands of approximately 85 kD on a Western blot (specification pg. 52, line 29 through pg. 53, line 7 and Fig. 6).

Applicants reserve the right to prosecute the non-elected claims and subject matter voluntarily removed from the pending claims in a divisional or continuation application filed during the pendency of the present application.

I. 35 USC §112, First Paragraph Rejection – New Matter

The examiner rejects pending claims 21 and 50 and their dependent claims for allegedly containing subject matter not described in the specification, i.e., new matter, in the pages of the Office Action spanning 6-11, specifically:

(a) Claims 21, 25 and 50 are rejected for use of language “said polypeptide isolatable from *Neisseria* bacteria”, and “*Neisseria* bacteria”, and use of “mammalian patient”;

(b) Claim 34 is rejected for use of “multiple *Neisseria* strains, said proteins appearing as reactive bands approximately 85 kD on a Western blot”;

(c) Claims 43 and 51 are rejected for use of “peptide lacking a signal sequence” because the examiner asserts that identifying the signal sequence in one of the OMP85 sequences of the specification is not sufficient to teach one of skill in the art that the identical sequence used in another OMP85 sequence which is 95% identical to the first sequence is also a signal sequence.

Applicants respectfully request reconsideration and withdrawal of these grounds for rejection in view of the above amendments and the following arguments. With regard to all rejections based on the language “at least 8 amino acids”, this language has been cancelled by the cancellation of claim 21, thereby rendering moot many of these outstanding rejections.

With regard to the rejection summarized in (a), claim 21 has been cancelled and claim 25 made dependent upon claim 50. The amendments to Claim 50 that identify the *Neisseria* bacteria and the assay are clearly supported in all priority documents. The term “mammalian patient” or subject is clearly supported by the use of a model mammalian patient in the generation of the antibodies used in Examples 7 and 8, and in the disclosure of the specification as referring to “mammals” (see, e.g., page 1, line 17). Applicants have further identified the mammalian cells exemplified in the assay as “epithelial” cells based on use of the well known Chang human epithelial cell model, which is a frequently used model cell line representative of mammalian epithelial cells. See, e.g., the publications Makino et al, 1991 EMBO J., 10(6):1307-1315 and Duensing et al, **Mar. 1997, Infect. Immun.**, 65(3):964-970, which are two examples of many publications in the art evidencing the use of the model mammalian epithelial cell line¹. Applicants have further referenced the assay in which this characteristic of the induced antibodies may be identified. All of these amendments are clearly supported in the specification and the priority documents.

¹ These documents are cited in the Supplemental Information Disclosure Statement filed herewith.

With regard to the rejection (b), amendment to the dependency of claim 34 is believed to moot this rejection.

Finally with regard to the examiner's continued rejection (c), Applicants maintain their previous argument. With respect, Applicants urge that the person of skill in the art given this specification which discusses the substantial similarity of these two proteins in both amino acid sequence and structure (particularly at the N termini of both proteins), and even designates both proteins by the same name, would clearly understand that the signal sequence of one such protein is a signal sequence of the other. The differences between the two sequences, both at the amino acid sequence and the gross structural level, would not be considered by one of skill in the art to change the function of the signal sequence from one OMP85 protein to the other.

None of this claim language is new matter. All is supported by the specification. This disclosure conveys *with reasonable clarity* to those skilled in the art, that, as of the filing date sought, Applicants were in possession of the invention of all pending claims. In summary, and as specified in the preceding response, Applicants' original specification clearly identifies SEQ ID NO: 2 and SEQ ID NO: 4 as homologous "OMP85" proteins having distinct structural similarities as well as having the ability to induce antibodies that are capable of recognizing a number of *Neisserial* OMP85 proteins. The term OMP85 is clearly used to refer to both SEQ ID NO: 2 and SEQ ID NO: 4. See, e.g., pg. 11, line 20 through pg. 12, line 10 and the comparison of the sequences in Fig. 5. The specification points to the similarities among the protein sequences (see pg. 16, lines 6-20), and the fact that the OMP85 *antigens* may be obtained as intact proteins, polypeptides or fragments, that such fragments may be as small as 5-8 consecutive amino acid sequences, and that such antigens or fragments share a biological activity, i.e., the ability to induce antibodies (pg. 18, line 27 through pg. 21, line 4; pg. 25, lines 14-15). That the OMP85 polypeptides and fragments can induce antibodies is taught at pg. 26, line 13 *et seq.* That such OMP polypeptides and fragments can be used diagnostically is described at pgs. 29-33. The OMP85 antigens and fragments, which can be immunogenic fragments (see pg. 35, line 20), can be used in compositions with

pharmaceutical carriers as taught at pgs. 33-37. The specification teaches that these proteins or fragments may be fused to other polypeptides by conventional means (pg. 21, line 25 through pg. 22, line 27).

Finally, the examples provide evidence that an illustrative antibody induced by an OMP85 protein fragment of amino acids 1-178 of SEQ ID NO: 2 which is virtually identical to the same sequence in SEQ ID NO: 4, but for 3 amino acids (see FIG. 5) induces antibodies that recognize or bind with the **both** OMP85 of SEQ ID NO: 2 and SEQ ID NO: 4. That the first 178 amino acids of SEQ ID NO: 4 can induce similarly reactive antibodies was demonstrated by the Declaration of Ralph C. Judd, that was submitted in this application with the response dated February 6, 2006. The specification clearly teaches that antibodies induced by an OMP85 antigen of this invention recognized the OMP85 protein in multiple *Neisseria* strains, i.e., from six representative strains of *N. gonorrhoeae* and four strains of *N. meningitidis*. See, pg. 48, lines 1-8 and FIG. 3. See, also, Example 7, at pgs. 50-52 and accompanying FIGs. 6, 7A and 7B. These examples clearly demonstrate that the OMP85 antigen can induce antibodies capable of binding the OMP85 proteins of multiple *Neisseria* strains, but **not** in the tested strains of *Klebsiella*, *Pseudomonas*, *Salmonella*, *Shigella* and *E. coli*. See pg. 52, last line through pg. 53, line 2. Example 8 at pg. 53 also teaches that the antibodies induced by the OMP85 polypeptide bind to the surface of bacteria and interfere with the ability of the bacteria to adhere to mammalian epithelial cells, as represented by the Change epithelial cell model employed in Example 8.

Again, the Examiner appears to reject the newly introduced claim language because the language is not present *in haec verba* in the specification. However, as clearly stated by the MPEP§2163, newly added claim limitations can be *implicitly or inherently* supported in the specification as well as by express disclosure. Also, MPEP §2163 at pg. 2100-183, col. 2 provides that to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference and that it would *be so recognized by persons of ordinary skill* (emphasis added). The fundamental factual inquiry for any written description rejection

is whether the specification conveys *with reasonable clarity* to those skilled in the art, that, as of the filing date sought, applicant was in possession of the invention as now claimed.

There is no reason, as required by MPEP§2163 at pg. 2100-176, col. 2, *why a person of skill in the art* would not recognize the support in the disclosure for all of the claim language, including that the signal sequence of the OMP85 from *Neisseria gonorrhoeae* in the identical position in the structurally similar OMP85 protein of *Neisseria meningitidis*, was a signal sequence, particularly given the remaining description of these proteins throughout the specification. With respect, Applicants submit that the examiner has not provided such reasoning.

Given the entirety of the specification and the understanding of the skilled artisan, it is respectfully submitted that all language used in independent claim 50 is understood by one of skill in the art as supported at least implicitly or inherently, if not explicitly, by the specification as filed.² As one example, one of skill in the art would understand that the identification of an “approximately 85kD” protein by identification on a Western blot is sufficiently clear for purposes of claims 34 and 44 to describe antibody binding. As another example, given the similarities of the sequences of SEQ ID NO: 2 and SEQ ID NO: 4 overall, as well as structural similarities of the OMP85 proteins, and the relative identity of the exemplified sequence used in the examples, one of skill in the art would understand that the signal sequence identified in FIG. 2 for SEQ ID NO: 2 is identical and in the identical position in the homologous OMP85 protein of SEQ ID NO: 4. Thus, the identification of that signal sequence and cleavage site in SEQ ID NO: 2 is inherent for the same sequence and cleavage site in SEQ ID NO: 4. One of skill in the art, given the present disclosure, would find inherent support for the claim language of claims 43 and 51. Similarly, given the description of the two OMP85 proteins, one of skill in the

² Even if every nuance of the claims is not explicitly described in the specification, the critical issue is the understanding of the skilled artisan. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991).

art would understand from the specification that a polypeptide 95% identical in sequence to SEQ ID NO: 4 is either SEQ ID NO: 4 or SEQ ID NO: 2.

Given the entirety of the specification, the preceding response which identified the supporting portions of the specification, and the understanding of the skilled artisan, it is respectfully submitted that none of the pending, rejected claims introduce new matter. In view of the amended language of the claims, and the clear support of the application for language currently employed in the claims, Applicants respectfully request that the examiner reconsider and withdraw this rejection as against any of the claims now pending.

II. 35 USC §112, Second Paragraph - Indefiniteness

Claims 21, 25-37, 39-46 and 50-52 are rejected as allegedly being indefinite in view of typographical and grammatical errors in claims 21 and 34, and use of "Neisseria bacteria" in the remaining claims

Applicants respectfully request reconsideration and withdrawal of these grounds for rejection in view of the amendment of the claims 34, 44 and 50, and the cancellation of claims 21 and 37. These claim amendments are believed to satisfy, and permit withdrawal of, this ground for rejection of all pending claims.

III. 35 USC §102(e)(2) Rejection

Claims 21, 25, 30-37 and 39-46 are rejected as allegedly anticipated by US 6,551,795 (Rubenfeld), as evidenced by Harlow et al. (In: Antibodies: A Laboratory Manual. Cold Spring Harbor Laboratory, Ch. 5, pg. 76, 1988).

Applicants respectfully request reconsideration and withdrawal of this rejection in view of the cancellation of independent claim 21, and the amendment of its dependent claims to become dependent upon claim 50, which is not rejected under this paragraph. Thus the amendments render this basis for rejection moot and not citable against any pending claim.

IV. 35 USC §102(b) Rejection

Claims 21, 25, 31-36, 39-42, 44-46 50, 52, and 53 are allegedly anticipated by Manning et al, Microb. Pathogen., 25:11-22 (1998), using Richarme et al, Ann. Microbiol. 133A:199204 (1982) to show that every element of the claimed subject matter is disclosed by Manning. The examiner applies this rejection, asserting that Applicants' pending claims are not entitled to their priority date and are permitted only the date of June 26, 2003.

Applicants respectfully request reconsideration and withdrawal of this rejection in view of the above claim amendments and remarks. As argued above, the pending claims do **not** introduce new matter over that disclosed in the present specification, but are fully supported by the pending specification. The pending specification is a *continuation* of the prior application No. 09/994,192 filed November 26, 2001, which is a *continuation* of the prior application No. 09/177,039, filed October 22, 1998. These applications have *the same* specifications with minor formal and grammatical corrections. Therefore, the present claims were similarly supported by these priority applications.

This rejection cannot stand as based on §102(b), because Manning was not published more than one year before October 22, 1998, and the previously filed *In re Katz* declaration appropriately moots any rejection which could only be based on §102(a), i.e., invention by “another”.

In view of the above amendments and remarks, Applicants respectfully request that the amended claims be permitted to issue in due course.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Deposit Account Number 08-3040.

Respectfully submitted,

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